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OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

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Subject: PP#: 5F6997. Myclobutanil. Human-Health Risk Assessment for Proposed Use on Soybeans. PC Code: 128857. DP#: 332919. Decision #: 361365.

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INTRODUCTION

Dow AgroSciences has submitted a petition for the use of myclobutanil [α-butyl-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile], formulated as Laredo® EW (EPA Reg. No. 62719-493), on soybeans. In addition, Dow has requested the establishment of permanent tolerances for the combined residues of myclobutanil and its metabolite, RH-9090 [α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile] 6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine], expressed as myclobutanil, in/on the following soybean raw agricultural commodities (RACs): soybean seed (0.05 ppm); soybean forage (5 ppm); soybean hay (13 ppm); soybean aspirated grain fractions (1.1 ppm); soybean hulls (0.06 ppm); soybean meal (0.03 ppm); and soybean oil (0.1 ppm).

NOTE: HED previously completed a Section 3 human-health risk assessment for the use of myclobutanil on hops and home gardens (Memo, J. Tyler, *et al.,* 7/12/06; D330235), and RD recently completed a Section 18 Emergency Exemption assessment for the use of myclobutanil on soybeans and legume vegetables (Memo, W. Cutchin, 8/9/05; D317318). The following information from the previous risk assessments on myclobutanil can be applied directly to this action:

- Residential Exposure Assessment (pages 12-17 of 7/12/06 memo).

In this memo, dietary, occupational and aggregate risks were re-evaluated based on the new use pattern for soybeans.

1.0 Executive Summary

Aggregate risk assessments were performed for acute (food and drinking water), short-term (food, drinking water and residential), intermediate-term (food, drinking water and residential), and chronic aggregate exposure (food and drinking water). The acute and chronic aggregate risks associated with the proposed uses of myclobutanil do not exceed HED's level of concern for the general U.S. population or any population subgroup. **Based upon a maximum turf application rate of 0.62-0.68 pound active ingredient (lb ai)/acre (A)**, the short-and intermediate-term aggregate margins of exposure (MOEs) are greater than 100 for the general U.S. population and all populations subgroups, including infants and children; and, therefore, do not exceed HED's level of concern (MOE <100).

HED Recommendations: Provided the Section F is revised (see Section 9.0), the residue chemistry, toxicological and occupational/residential databases are adequate to support the establishment of a conditional registration and permanent tolerances for the combined residues of myclobutanil and its alcohol metabolite α- (3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile (free and bound) in/on soybean, seed (0.25 ppm); soybean, forage (3.5 ppm); soybean, hay (15 ppm); aspirated grain fractions (35 ppm), and soybean, refined oil (0.40 ppm). The registration may be made unconditional upon submission of the requested information from the processed food and feed study.

It should be noted that the previous human-health risk assessment (Memo, J. Tyler, *et al.,* 7/12/06; D330235) included two application rates for the residential turf use – 1.36 and 0.62 lb ai/A. In that assessment, the short- and intermediate-term aggregate MOE for children/toddlers exceeded HED's level of concern for the "playing on lawn" scenario using the turf application rate of 1.36 lb ai/A, but did not exceed HED's level of concern for the same scenario using the 0.62 lb ai/A turf application rate. Since the completion of the 7/12/06 risk assessment, the company has revised all residential turf labels to include a maximum application rate of 0.62-0.68 lb ai/A (personal communication between J. Tyler and L. Jones, 10/3/06). Therefore, the high rate of 1.62 lb ai/A was removed from the residential exposure assessment, resulting in aggregate short- and intermediate-term MOEs of >100 for children/toddlers. **RD should ensure that all myclobutanil labels with residential turf uses have been revised to include a maximum application rate of 0.62-0.68 lb ai/A.** Additionally, the slight increase in application

rate (*i.e.* 0.62 lb ai/A to 0.68 lb ai/A) will not have a significant effect on the results of the risk assessment. The short- and intermediate-term aggregate MOEs are greater than 100 for the general U.S. population and all populations subgroups, including infants and children; and, therefore, do not exceed HED's level of concern (MOE <100).

In addition, it should be noted that the proposed label includes a restriction on feeding treated soybean forage and hay to livestock. The registrant has stated that this restriction is a misprint, and will be removed (personal communication between R. Brinkmeyer and J. Tyler, 10/12/06). **RD should ensure that a revised Section B is submitted.**

HED suggests that the RD confirm or correct, as may be necessary, the 24-hour restricted entry interval (REI) listed on the product label.

2.0 Ingredient Profile

2.1 Summary of Registered/Proposed Uses

Registered Uses: Myclobutanil is a contact fungicide that is applied to prevent fungal outbreaks. In agricultural and commercial settings, it has a variety of uses including fruits, vegetables, ornamentals, and turf. In the residential setting, the existing uses include turf and ornamentals. Permanent tolerances are currently established for the combined residues of myclobutanil and its RH-9090 metabolite (free and bound) in/on a variety of RACs at levels ranging from 0.02 to 25.0 ppm and in meat, milk, poultry, and eggs at levels ranging from 0.02 to 1.0 ppm [40 CFR §180.443(a)]. In addition, tolerances in conjunction with Section 18 registrations have been established for a number of RACs under 40 CFR §180.443(b). Tolerances for indirect or inadvertent residues of myclobutanil have been established for several crop groups under 40 CFR §180.443(d).

Proposed Uses: A specimen label was provided for Laredo® EW, a product containing 1.67 lb ai/gallon (gal). Table 2.1.1 is a summary of the proposed use pattern.

Table 2.1.1. Summary of Proposed Use Pattern.

Crop	Product (EPA Reg. No.)	# App.	Application Rate (lb ai/A)		RTI[1] (days)	PHI[1] (days)	REI[1] (hours)	Restrictions
			Per app.	Per season				
Soybean	62719-493	2	0.0625-0.125	0.25	14-21	28	24	Use adequate spray volume to achieve good coverage and canopy penetration (for ground applications, typically 15-20 GPA; for aerial applications, typically a minimum of 5 GPA).

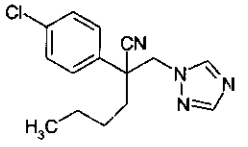
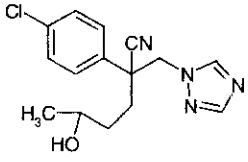
[1] RTI = retreatment interval; PHI = preharvest interval; REI = restricted-entry interval.

The label specifies the following rotational crop restrictions: Fields treated with myclobutanil can be rotated at any time to crops that are listed on a registered myclobutanil label immediately after the last treatment. Do not plant other crops within 30 days after the last application of a product containing myclobutanil. The proposed use directions are adequate and supported by the available residue chemistry data. It should be noted that the proposed label includes a restriction

on feeding treated soybean forage and hay to livestock. However, the registrant has stated that this restriction is a misprint, and will be removed (personal communication between R. Brinkmeyer and J. Tyler, 10/12/06). **RD should ensure that a revised Section B is submitted.**

2.2 Structure and Nomenclature

Table 2.2.1. Myclobutanil Nomenclature.

Chemical structure	
Common name	Myclobutanil
Company experimental name	RH-3866
IUPAC name	(*RS*)-2-(4-chlorophenyl)-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile
CAS name	∝-butyl-∝(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile
CAS #	88671-89-0
End-use product/(EP)	The trade name of the product used was Systhane® 20EW, but will marketed as Laredo® EW Fungicide
Chemical structure of regulated metabolite	
Common name	Alcohol metabolite
Company experimental name	RH-9090

2.3 Physical and Chemical Properties

Table 2.3.1. Physicochemical Properties of the Technical Myclobutanil.

Parameter	Value	Reference
Melting point range	63-68 °C	Product Chemistry Review (C.L. Trichilo, 1988), and Rohm and Haas Report, "Revision to: RH-3866 Technical - Physical and Chemical Characteristics"
pH	The technical material cannot be diluted or dispersed in water. The pH of a saturated aqueous solution of this material is about 6-7, the same as the background value of the water used.	
Density	1.22 g/cc @ 23 °C 1.19 g/cc @ 100 °C	
Water solubility (20 °C)	(25 °C) 142 ppm	
Solvent solubility (g/L at 20 °C)	xylene: >50 g/100g amyl acetate: >50 g/100g cyclohexanone: >50 g/100g DMF: >50 g/100g methyl ethyl ketone: >50 g/100g	
Vapor pressure at 20 °C	1.6 X 10-6 torr @ 25 °C for pure ai	
Dissociation constant, pK_a	The pure ai does not have acidic hydrogens and is expected to be a very weak base. Attempts to measure pKa by titration with acid (HCl) and base (NaOH) failed to detect any inflection on the titration curve, indicating little or no dissociation.	
Octanol/water partition coefficient $Log(K_{OW})$	2.94 @ 25 °C for pure ai	
UV/visible absorption spectrum	not available	

3.0 Hazard Characterization/Toxicity Endpoint Selection

3.1 Hazard Characterization: The toxicological database for myclobutanil is adequate to support registration and tolerances. There are no data gaps. Myclobutanil has low acute toxicity with the exception for ocular irritation. It is Toxicity Category III for oral acute toxicity, and Category IV for dermal and inhalation acute toxicity and dermal irritation. Myclobutanil is Category I for ocular irritation and the technical is a dermal sensitizer. However, the formulation containing 40% myclobutanil was not sensitizing. In rat subchronic and chronic toxicity studies, the primary target organs are liver and testes. Liver effects, following subchronic exposure, include hypertrophy, hepatocellular necrosis and increased liver weight. There is decreased testicular weight and testicular atrophy. Chronic exposure to the rat also results in hepatocellular vacuolization and additional testicular effects, which include bilateral aspermatogenesis, increased incidences of hypospermia and cellular debris in the epididymides and increased incidences of arteritis/periarteritis in the testes. With the exception of testicular effects, subchronic and chronic exposures in the mouse result in a toxicity profile similar to the rat. The mouse, following chronic exposure, has, in addition, increased Kupffer cell pigmentation, periportal punctate vacuolation, and individual cell necrosis of the liver. There is no evidence of carcinogenic potential in either the rat or mouse. In the subchronic dog, there are hepatocellular hypertrophy, increased relative and absolute liver weight and increased alkaline phosphatase. In the chronic dog study, liver toxicity is similar with the addition of "ballooned" hepatocytes and increases in SGPT and GGT. Signs of toxicity observed in the rat 28-day dermal studies (studies on the 40WP and 2EC formulations) are limited to dermal irritation. There is no evidence of systemic toxicity in either study. There is no evidence of increased susceptibility in either of the developmental toxicity studies or the reproduction study. In the rat developmental toxicity study, maternal toxicity, which included rough hair coat and salivation, occurs at the same dose level as increases in incidences of 14^{th} rudimentary and 7^{th} cervical ribs in the fetuses. At the next higher dose there is also alopecia, desquamation and red exudate around the mouth in the dams. In the rabbit developmental toxicity study there is reduced body weight and body weight gain during the dosing period, clinical signs of toxicity and a possible increase in abortions in the does at the same dose level that there are increased resorptions, decreased litter size and decreased viability index. The maternal toxicity in the rat reproduction study includes increased liver weights and hepatocellular hypertrophy. Reproductive effects occur at the same dose and include increased incidences in the number of still born pups and atrophy of the testes, epididymides and prostate. Developmental effects occurring at the same dose in the reproduction study include decreased pup body weight gain during lactation. Myclobutanil is rapidly absorbed and excreted with complete elimination by 96 hours. There is extensive metabolism prior to excretion with elimination of radiolabeled material evenly distributed between urine and feces. There is no evidence of tissue accumulation. There is no concern for mutagenic activity. Myclobutanil was determined to be not carcinogenic in two acceptable animal studies. Therefore, it was classified as a "Group E" chemical (evidence of noncarcinogenicity for humans).

3.2 Toxicity Endpoint Selection: The doses and toxicological endpoints selected for various exposure scenarios are summarized in Table 3.2.1. RAB1 toxicologists recently re-evaluated the myclobutanil toxicology database and concluded that the 28-day dermal toxicity study previously used for short-term dermal risk assessment is not appropriate (Memo, J. Tyler, *et al.*, 7/12/06; D330235). A two-generation reproduction study in rats was selected because the effects of concern (atrophy of the testes and prostate) seen at a lowest observed adverse effect level (LOAEL) of 50 mg/kg/day may not be protective if the endpoints were based on the 28-day dermal toxicity study. In addition, there were no effects of concern identified in the 28-day dermal toxicity study [no observed adverse effect level (NOAEL) of 100 mg/kg/day was the highest dose tested].

Table 3.2.1. Summary of Toxicological Dose and Endpoints for Myclobutanil for Use in Human Risk Assessment.

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects
Acute Dietary females 13-50 years of age	NOAEL = 60 mg/kg/day UF = 100 **Acute RfD** = 0.60 mg/kg/day	FQPA SF = 1x **aPAD** = acute RfD / FQPA SF = 0.60 mg/kg/day	Developmental Toxicity - rabbit[1] LOAEL = 200 mg/kg/day based on increased resorptions, decreased litter size and a decrease in the viability index.
Acute Dietary general population including infants and children	None	not applicable	not applicable
Chronic Dietary all populations	NOAEL= 2.49 mg/kg/day UF = 100 **Chronic RfD** = 0.025 mg/kg/day	FQPA SF = 1x **cPAD** = chronic RfD / FQPA SF = 0.025 mg/kg/day	Chronic Toxicity/ Carcinogenicity - rat LOAEL = 9.94 mg/kg/day based on decreased testicular weights and increased testicular atrophy.
Short-Term Dermal (1-30 days) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (dermal absorption rate = 50%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Intermediate-Term Dermal (1-6 months) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (dermal absorption rate = 50%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Long-Term Dermal (> 6 months) (Occupational/ Residential)	oral study NOAEL= 2.49 mg/kg/day (dermal absorption rate = 50%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	Chronic Toxicity/ Carcinogenicity – rat LOAEL = 9.94 mg/kg/day based on decreased testicular weights and increased testicular atrophy.

Table 3.2.1. Summary of Toxicological Dose and Endpoints for Myclobutanil for Use in Human Risk Assessment.

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects
Short-Term Inhalation (1-30 days) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Intermediate-Term Inhalation (1 –6 months) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Long-Term Inhalation (>6 months) (Occupational/ Residential)	oral study NOAEL= 2.49 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	Chronic Toxicity/ Carcinogenicity - rat LOAEL = 9.94 mg/kg/day based on decreased testicular weights and increased testicular atrophy.
Cancer (oral, dermal, inhalation)	"Group E"	not applicable	not applicable

1. The HIARC document (dated 9/2/99) table incorrectly lists this as rat.

4.0 Food Quality Protection Act (FQPA) Assessment

The FQPA Safety Factor Committee (SFC) met on August 16, 1999 (HED Doc. No. 013734, dated 9/13/99) to evaluate the hazard and exposure data for myclobutanil. The committee recommended that the FQPA Safety Factor (SF) (as required by FQPA of August 3, 1996) be reduced to 1x in assessing the risk posed by this chemical. The myclobutanil risk assessment team has re-evaluated the quality of the toxicology and exposure data; and, based on these data, recommended that the FQPA SF be reduced to 1x. The recommendation is based on the following:

- There are no toxicity data gaps in the consideration of the FQPA SF.
- The Hazard Identification Assessment Review Committee (HIARC) concluded that there was no evidence of increased susceptibility in the developmental toxicity studies with rats and rabbits.
- HIARC determined that a developmental neurotoxicity study is not required because neurotoxic compounds of similar structure were not identified and there was no evidence of neurotoxicity in the current toxicity database.
- The exposure assessments will not underestimate the potential dietary (food and drinking water) and residential (non-occupational) exposures for infants and children from the use of myclobutanil.
- The acute dietary food exposure assessment (females 13-49 years old only) utilizes existing and proposed tolerance level residues and 100% crop treated (CT) information for all commodities. By using these screening-level assessments, actual exposures/risks will not be underestimated.
- The chronic dietary food exposure assessment utilizes existing and proposed tolerance level residues; United States Department of Agriculture (USDA) Pesticide Data Program (PDP) monitoring data for apple juice,

bananas (not plantains) and milk; average % CT data verified by the Biological Economic and Analysis Division (BEAD) for apple (except juice), apricots, artichokes, asparagus, sugar beet, blackberry, and tomatoes; and 100% CT information for all other registered and proposed uses. The chronic assessment is somewhat refined and based on reliable data and will not underestimate exposure/risk.

- The dietary drinking water assessment utilizes water concentration values generated by model and associated modeling parameters, which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded.
- The residential handler assessment is based upon the residential standard operating procedures (SOPs) and utilized unit exposure data from the Outdoor Residential Exposure Task Force (ORETF) and the Pesticide Handlers Exposure Database (PHED). The residential post-application assessment is based upon chemical-specific turf transferable residue (TTR) data and DFR data. The chemical-specific study data as well as the surrogate study data used are reliable and also are not expected to underestimate risk to adults as well as to children. In a few cases where chemical-specific data were not available, the SOPs were used alone. The residential SOPs are based upon reasonable "worst-case" assumptions and are not expected to underestimate risk. These assessments of exposure are not likely to underestimate the resulting estimates of risk from exposure to myclobutanil.

5.0 Endocrine Disruption

EPA is required under the Federal Food Drug and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate. "Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there were scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA has authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, myclobutanil may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

6.0 Exposure Characterization/Assessment

The residue chemistry data submitted in support of proposed petitions were summarized in the HED-memorandum dated 10/18/06 (J. Tyler; DP# 323503). A drinking water assessment was provided by the Environmental Fate and Effects Division (EFED) in a memorandum dated 6/26/06 (J. Wolf, DP# 329419). An acute and chronic dietary exposure assessment was completed in a HED-memorandum dated 10/18/06 (J. Tyler, DP# 322917). A residential exposure assessment was conducted in conjunction with the request for the use of myclobutanil on hops and home gardens (Memo, T. Dole, 2/8/06; D319227).

5.1 Dietary Exposure/Risk Pathway

5.1.1 Residue Profile

Nature of the Residue in Plants and Livestock Commodities: Plant metabolism studies on wheat, grapes, and apples have previously been submitted, and were reviewed and summarized in HED review of PP#2F4155 (Memo, D. Davis, 2/8/93; D183273). The requirement to conduct a tomato metabolism study, in conjunction with PP#1F4030, was waived (DP Barcode D203587, J. Stokes, 7/13/94). By translation of metabolism data from wheat, the qualitative nature of the residue in soybeans is adequately understood. The residues of concern are the parent myclobutanil and its RH-9090 metabolite (free and bound).

Myclobutanil metabolism in meat, milk, poultry, and eggs has been reviewed in conjunction with PP#7F3476 (Memo, M. Nelson, 2/8/88) and summarized in conjunction with the temporary tolerance petition for almond nuts and hulls (PP#9G3786, Memo, J. Smith, 12/6/89). The nature of the residue in livestock is adequately understood. The residues of concern in livestock commodities except milk are myclobutanil and its metabolite α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile (free). The residues of concern in milk are myclobutanil [α-butyl-α-(4-chlorophenyl)-1*H* -1,2,4-triazole-1-propanenitrile] and its metabolites, α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile (free and bound) and α-(4-chlorophenyl)-α-(3,4-dihydroxybutyl)-1*H* -1,2,4-triazole-1-propanenitrile.

Analytical Methodology: An adequate enforcement method (Rohm and Haas Method 34S-88-10, MRID# 408033-02) is available to enforce the proposed tolerances on soybeans. Quantitation is by GLC using a nitrogen/phosphorus (N/P) detector for myclobutanil and an electron capture detector (Ni^{63}) for residues measured as the alcohol metabolite. HED has conducted a successful method validation of Method 34S-88-10, and the method has been forwarded to the Food and Drug Administration (FDA) for inclusion in Pesticide Analytical Method Volume II (PAM) Vol. II (PP#7F3476 and FAP#7H5524, M. J. Nelson, 4/14/88 and 7/18/89). Samples from the crop field and processing studies were analyzed for residues of myclobutanil and its alcohol metabolite RH-9090 using analytical method GRM 05.07. Briefly, residues of myclobutanil and its alcohol metabolite RH-9090 were extracted from soybean samples by homogenizing and shaking overnight with methanol. An aliquot was hydrolyzed to release conjugated RH-9090 by adding concentrated hydrochloric acid (HCl) and heating for 2 hours at approximately 70 °C. The pH was adjusted to near neutral using 0.5 M aqueous base. The sample was then filtered, and the final solution analyzed using on-line solid-phase extraction coupled to high-performance liquid chromatography with positive-ion atmospheric pressure chemical ionization (APCI) tandem mass spectrometry (HPLC/MS/MS). The limit of detection (LOD) and limit of quantitation (LOQ) for all soybean matrices were determined to be 0.003 and 0.01 ppm, respectively.

Enforcement methods for the established tolerances on livestock commodities are Methods 34S-88-22 (MRID #408253-01), 34S-88-15 (MRID #406458-01), 31S-87-02 (MRID #404813-01), and 34S-88-21 (MRID #408033-01). These methods have been submitted for publication in PAM II (PP#7F3476, M.J. Nelson, 7/18/89).

The 2/97 FDA PESTDATA database (PAM Volume I, Appendix I) indicates that residues of myclobutanil are adequately recovered (>80%) using Multiresidue Method Section 302 (Luke Method; Protocol D), but are not recovered using Multiresidue Method Sections 303 (Mills, Onley, Gaither Method; Protocol E, non-fatty foods) or 304 (Mills Method; Protocol E, fatty foods). Residues of the metabolite RH-9090 were poorly recovered (30-55%) using Multiresidue Method Section 302 (Luke Method; Protocol D); the metabolite is not recovered using Multiresidue Method Sections 303 (Mills, Onley, Gaither Method; Protocol E, non-fatty foods) and 304 (Mills Method; Protocol E, fatty foods).

Storage Stability: The maximum storage intervals for treated samples in the crop field trial study were 216, 218, and 137 days for soybean forage, hay, and seed, respectively. Adequate storage stability studies for myclobutanil on apples and grapes have been reviewed by HED (Memo, M. Nelson, 2/8/88; Accession#s 266109 & 266115). In another submission, apples and grapes were reanalyzed for myclobutanil and its metabolite after frozen storage (Memo, M. Nelson, 4/26/88). Grapes and apples treated with myclobutanil, harvested, analyzed, and stored over 3 years and reanalyzed for both myclobutanil and its metabolite showed no change in the levels or composition of the residues demonstrating the long-term stability of myclobutanil and its metabolite in samples for at least 3 years under frozen conditions. Additional storage stability studies demonstrate that myclobutanil and its alcohol metabolite are stable under frozen conditions for the following time periods: 288 days in/on asparagus (Memo, G. Kramer, 12/11/98; D238442); 657 days (22 months) in/on snap beans (Memo, N. Dodd, 4/24/98; D238454); 296 days in/on mint (Memo, J. Rowell, 8/3/99; D238448); and 36 months in/on tomatoes (Memo, J. Rowell, 9/13/99; D251632). The available storage stability data are adequate to support crop field trial data. **However, information on the maximum storage intervals of samples in the processed food and feed study, from harvest to analysis, for soybean seed (RAC), hulls, meal and refined oil should be provided.**

Magnitude of the Residue in Livestock: The established ruminant tolerances are based on an estimate of the maximum theoretical dietary burden (MTDB) of myclobutanil and its alcohol metabolite RH-9090 (free and bound) of 23.2 ppm, which was based on a hypothetical diet of almond hulls, grape pomace (wet), and raisin waste (Memo, M. Peters, 2/17/94; D193006). The poultry tolerances are based on an estimated MTDB of 0.75 ppm, which is based on a hypothetical diet of apple and grape pomace (Memo, M. Nelson, 4/26/88). Grape pomace and raisin wastes are not currently considered to be livestock feed items (Table 1 of OPPTS Residue Chemistry Test Guidelines OPPTS 860.1000). The livestock feed items associated with the proposed use include soybean seed, forage, hay, aspirated grain fractions, meal, hulls, and silage. An updated calculation of the MTDB resulted in dietary burdens of 13.5 ppm, and 0.074 ppm for beef and dairy cattle, and poultry. As these dietary burdens do not exceed the MTDB (23.2 ppm and 0.75 ppm for cattle/hogs and poultry, respectively) used to determine the current tolerances for livestock commodities, an increase in ruminant and poultry tolerances is not needed to support this action.

Magnitude of the Residue in Plants: The crop field trial data for soybeans are classified as acceptable and satisfy the guideline requirement for crop field trials (Residue Chemistry Guidelines OPPTS 860.1500). Following 2 foliar applications of GF-1062 (an EW formulation containing 19% myclobutanil as the ai) 0.125 lb ai/A (total application rate of 0.250 lb ai/A; 1x the maximum proposed seasonal application rate), the maximum combined residues of myclobutanil and its alcohol metabolite RH-9090 in soybean hay, forage, and seed were 3.4354 ppm, 11.4364 ppm, and 0.2090 ppm, respectively (with 12- to 17-day RTI and a 14-day PHI). The forage decline study indicates that residues of myclobutanil decline steadily with a half-life of 7-9 days; RH-9090 residues increase from the day of application until day-7 then gradually declined. Although the samples were harvested at 14-day PHI and the proposed PHI is 28 days, the available residue decline data on forage indicate that residues of myclobutanil decline steadily with a half-life of 7-9 days, and RH-9090 decline steadily after Day-7. Therefore, the residue data support the establishment of permanent tolerances for the residues of myclobutanil and its alcohol metabolite (free and bound) in/on soybean, forage at 3.5 ppm; soybean, hay at 15 ppm; and soybean, seed at 0.25 ppm. **A revised Section F should be submitted.**

Magnitude of the Residue in Processed Commodities: Under the conditions and parameters used in the study, the processed food and feed data are classified as scientifically acceptable, with the exception of the aspirated grain fraction (AGF) data. The results of the processing study indicate that, following 2 foliar applications of GF-1062 at 0.625 lb ai/A/application (total application rate of approximately 1.25 lb ai/A; 5x the maximum proposed seasonal application rate; 10- to 15-day RTI and 14-day PHI), residues of myclobutanil and RH-9090 do not appear to concentrate in soybean hulls (1.1x) and soybean meal (0.52x). Residues of myclobutanil and RH-9090 do appear to concentrate in soybean refined oil (2.0x) and soybean AGF (70x) processed from soybean seeds bearing detectable residues. The maximum theoretical concentration factor for soybean is 12x (OPPTS 860.1520, Table 1), and 11.3x, 2.2x, and 12.0x for hulls, meal, and oil, respectively, based on separation into components (OPPTS 860.1520, Table 3). Therefore, tolerances on soybean hulls and meal are not necessary.

For refined oil, using the HAFT of 0.1687 ppm for soybean seed from the crop field trial study, the maximum expected residue level in soybean refined oil would be 0.34 ppm (0.1687 ppm x 2.0). Therefore, an appropriate tolerance for residues of myclobutanil and it alcohol metabolite (free and bound) in/on soybean, refined oil is 0.40 ppm. **A revised Section F should be submitted.**

For AGF, the particle size distribution sample does not match what is typically used in commercial practices. The AGF particle sizes were classified as follows: >2360 micron (82.3%), >2000 micron (0.3%), >1180 micron (0.8%), >850 micron (0.4%), >425 micron (0.5%), and <425 micron (15.6%). According to current OPPTS guidelines, the dust should be fractionated into four or five different ranges. The purpose of this distribution data is to show that the AGF typifies a sample of commercial elevator AGF, which at least 50% has a particle size of <400 μm. Therefore, as a worst-case scenario, it was assumed that all residues were in the particle sizes of <425 μm. Therefore, if residues of myclobutanil concentrated 70x when 15.6% of the AFG was <425 μm, then residues would presumably be ~ 200x (70 x 3) when 50% (15.6% x 3) of the AGF has a particle size of <425 μm. Using the HAFT of 0.1687 ppm for

soybean seed from the crop field trial data, the maximum expected residue level in AGF is 34 ppm (0.1687 ppm x 200). Therefore, the appropriate tolerance for residues of myclobutanil and it alcohol metabolite (free and bound) in/on aspirated grain fractions is 35 ppm. **A revised Section F should be submitted.**

Confined/Field Accumulation in Rotational Crops: The proposed label includes the following restriction: Fields treated with myclobutanil can be rotated at any time to crops that are listed on a registered label immediately after the last treatment. Do not plant other crops within 30 days after the last application of a product containing myclobutanil. The current rotational crop restrictions are adequate, and are supported by previously-reviewed limited field rotational crop study conducted at a total application rate of 0.75 lb ai/A (3x the maximum season application rate for soybeans) (Memo, J. Tyler; DP# 308904; MRID 46034003).

Recommendations for Tolerances/International Considerations: A summary of the recommended tolerances and the correct commodity definitions for the proposed uses are listed in Table 5.1.1. The appropriate tolerance levels were calculated using the methodology formulated by the North America Free Trade Agreement (NAFTA) Maximum Residue Limit (MRL)/Tolerance Harmonization Workgroup for calculating statistically based pesticide tolerances for plant commodities based on field trial residue data.

Table 5.1.1. Tolerance Summary for Myclobutanil.

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments (*correct commodity definition*)
Soybean seed	0.05	0.25	*Soybean, seed*
Soybean forage	5	3.5	*Soybean, forage*
Soybean hay	13	15	*Soybean, hay*
Soybean aspirated grain fractions	1.1	35	*Aspirated grain fractions*
Soybean hulls	0.06	-	Based on available processing data, a tolerance on soybean hulls is not needed.
Soybean meal	0.03	-	Based on available processing data, a tolerance on soybean meal is not needed.
Soybean oil	0.1	0.40	*Soybean, refined oil*

There are no current Codex, Canadian or Mexican maximum residue limits (MRLs) for residues of myclobutanil in/on soybeans. Therefore, harmonization is not an issue.

5.1.2 Drinking Water Considerations

EFED provided Estimated Drinking Water Concentrations (EDWCs) of myclobutanil in surface and ground water using PRZM-EXAMS and Screening Concentration in Ground Water (SCI-GROW), respectively. The assessment was based on hops, which has the highest use rate among all existing uses. EFED calculated the 1- in 10-year peak acute and 1- in 10-year estimated annual mean non-cancer chronic EDWCs for myclobutanil in surface water to be 15.3 ppb and

8.5 ppb, respectively. The ground water EDWC for both acute and chronic exposures is estimated as 0.35 ppb.

It should be noted that in the 7/12/06 human-health risk assessment (Memo, J. Tyler, *et al.*, 7/12/06; D330235), HED used ground and surface water EDWCs provided by EFED in a memo dated 6/9/03 (T. Nguyen; D290167 and D289700). The acute (peak) and chronic (56-day) EDWCs for myclobutanil in surface water [using FQPA Index Reservoir Screening Tool (FIRST)] were 333 ppb and 86 ppb, respectively. The ground water EDWC (using SCI-GROW) for both acute and chronic exposures was estimated as 3.2 ppb. The 6/9/03 drinking water assessment was also based on hops. However, the major reason for difference between the current EDWCs compared to the 6/9/03 assessments is due to changes in application rates to hops. The previous assessment was based upon 15 applications at 0.65 lb ai/acre with 14 day RTIs (total 9.75 lb ai/acre/year), while the current maximum application rate is 1.0 lbs ai/acre/year.

5.1.3 Dietary Risks (Food and Drinking Water)

Acute (females 13-49 years old) and chronic dietary exposure (general U.S. population and all population subgroups) assessments were conducted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™; ver. 2.03) program which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (*e.g.*, apple pie) are linked to EPA-defined food commodities (*e.g.* apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA and EPA. Consumption data are averaged for the entire U.S. population and within population subgroups for chronic exposure assessment, but are retained as individual consumption events for acute exposure assessment.

For chronic exposure and risk assessment, an estimate of the residue level in each food or food-form (*e.g.*, orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form. The resulting residue consumption estimate for each food/food form is summed with the residue consumption estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the chronic population adjusted dose (cPAD). This procedure is performed for each population subgroup.

For acute exposure assessments, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic (Tier 1 or Tier 2) exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic (Tier 3/4) assessment. The resulting distribution of exposures is expressed as a percentage of the acute population adjusted dose (aPAD) on both a user (*i.e.*, those who reported eating relevant commodities/food forms) and a per-capita (*i.e.*, those who reported eating the relevant commodities as well as those who did not)

basis. In accordance with HED policy, per capita exposure and risk are reported for all tiers of analysis. However, for Tiers 1 and 2, significant differences in user vs. per capita exposure and risk are identified and noted in the risk assessment.

HED's level of concern is when the exposure is greater than 100% of the PAD. That is, estimated exposures above this level are of concern, while estimated exposures at or below this level are not of concern. The DEEM-FCID™ analysis estimates the dietary exposure of the U.S. population and 26 population subgroups. The results reported in Table 5.1.3.1 are for the U.S. population, all infants (<1 year old), children 1-2 years old, children 3-5 years old, children 6-12 years old, youth 13-19 years old, females 13-49 years old, males 20-49 years old, and adults 50+ years old.

***Acute Dietary Exposure Estimates*:** An acute dietary exposure assessment was performed for females 13-49 years old (no endpoint was identified for the general U.S. population or any other population subgroup) using tolerance-level residues and 100% CT information for all registered and proposed uses. Drinking water was incorporated directly in the dietary assessment using the acute (peak) concentration for surface water generated by the PRZM-EXAMS model. These assessments conclude that the acute dietary exposure estimates (95th percentile) are below HED's level of concern (<100% of the aPAD) for females 13-49 years old at 2.4% of the aPAD.

***Chronic Dietary Exposure Estimates*:** A refined, chronic dietary exposure assessment was performed for the general U.S. population and various population subgroups using USDA PDP monitoring data for apple juice, bananas (not plantains) and milk, registered and proposed tolerance for all other commodities; average % CT information for apple (except juice), apricots, artichokes, asparagus, sugar beet, blackberry, and tomatoes; and 100% CT information for all other registered and proposed uses. Drinking water was incorporated directly into the dietary assessment using the chronic concentration for surface water generated by the PRZM-EXAMS model. This assessment concludes that the chronic dietary exposure estimates are below HED's level of concern (<100% of the cPAD) for the general U.S. population (10% of the cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old at 24% of the cPAD.

Table 5.1.3.1. Summary of Dietary Exposure and Risk for Myclobutanil.

Population Subgroup	Acute Dietary[1]		Chronic Dietary[2]	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD
U.S. Population (total)	NA		0.002587	10
All Infants (< 1 year old)			0.004280	17
Children 1-2 years old			**0.006129**	**24**
Children 3-5 years old			0.005090	20
Children 6-12 years old			0.003314	13
Youth 13-19 years old			0.002041	8.2
Adults 20-49 years old			0.002182	8.7
Adults 50+ years old			0.002222	8.9
Females 13-49 years old	**0.14279**	**2.4**	0.002089	8.4

[1] Acute dietary endpoint of 0.6 mg/kg/day for females 13-49 years old. No acute dietary endpoint was chosen for the general U.S. population, including infants and children.
[2] Chronic dietary endpoint of 0.025mg/kg/day applies to the general U.S. population and all population subgroups.

5.2 Residential Exposure

All residential handler exposures and risks resulted in MOEs of >100; and, therefore, do not exceed HED's level of concern. The residential handler assessment was based upon the residential SOPs, PHED data, and ORETF study data. All residential post-application exposures and risks resulted in MOEs of >\100; and, therefore, do not exceed HED's level of concern. The residential post-application assessment was based upon standard assumption from residential SOPs, the results of two dislodgeable foliar residue (DFR) studies on grapes in California, and TTR data, when applicable.

It should be noted that the previous residential post-application exposure assessment included two application rates for the turf use – 1.36 and 0.62 lb ai/A. The myclobutanil MOEs for toddler exposures at day 0, expressed as the total MOE, exceeded HED's level of concern (MOE<100) when the application rate is 1.36 lb ai/A, but did not exceed HED's level of concern (MOE>100) when the application rate is 0.62 lb ai/A. Since the completion of the 7/12/06 risk assessment, the company has revised all turf labels to include a maximum application rate of 0.62-0.68 lb ai/A (personal communication between J. Tyler and L. Jones, 10/3/06). Therefore, the high rate of 1.62 lb ai/A has been removed from the residential assessment, and all residential post-application exposures and risks resulted in MOEs of >100.

6.0 Aggregate Risk

Aggregate risk assessments were performed for acute (food and drinking water), short-term (food, drinking water and residential), intermediate-term (food, drinking water and residential), and chronic aggregate exposure (food and drinking water). Long-term and cancer aggregate risk assessments were not performed because, based on the current and proposed use patterns, HED does not expect residential exposure durations that would result in long-term exposures and myclobutanil is not carcinogenic. All potential exposure pathways were assessed in the aggregate risk assessment.

6.1 Acute Aggregate Risk Assessment (Food and Drinking Water): The acute aggregate risk assessment takes into account exposure estimates from dietary consumption of myclobutanil (food and drinking water). Dermal, inhalation, and incidental oral exposures resulting from short-term residential applications are assessed separately. The acute dietary exposure estimates are below HED's level of concern (<100% aPAD) at the 95th exposure percentile for females 13-49 years old (2.4% of the aPAD; see Table 5.1.3.1). Therefore, the acute aggregate risk associated with the proposed uses of myclobutanil does not exceed HED's level of concern for females 13-49 years old.

6.2 Short-Term Aggregate Risk Assessment (Food, Drinking Water and Residential): The short-term aggregate risk assessments estimate risks likely to result from 1-30 days of exposure to myclobutanil residues in food, drinking water, and residential pesticide uses. In aggregating short-term risk, HED considered background chronic dietary exposure (food and drinking water; see Table 5.1.3.1) and short-term, non-dietary oral and/or dermal exposures.

For adults, there is potential for short-term dermal and inhalation handler exposure, and short-term dermal post-application exposures from the residential uses of myclobutanil, including orchards, "pick your own" gardens, home fruit and vegetable gardens, and treated turf. However, the handler and post-application exposures were not combined as the likelihood of the residential homeowner experiencing both short-term handler and post-application exposure to myclobutanil is unlikely [it is current HED Science Advisory Council for Exposure (ExpoSAC) policy not to combine handler and post-application exposures for these scenarios due to the conservative nature of each assessment alone]. For children/toddlers, short-term dermal and non-dietary oral post-application exposures may result from dermal contact with treated turf as well as non-dietary ingestion/hand-to-mouth transfer of residues from turf grass.

For the general U.S. population and children/toddlers, the total food and residential short-term aggregate MOEs are listed in Table 6.3.1. For the general U.S. population and all population subgroup, including infants and children, all short-term MOEs are greater than 100; and, therefore, do not exceed HED's level of concern (MOE <100).

6.3 Intermediate-Term Aggregate Risk Assessment (Food, Drinking Water and Residential): The intermediate-term aggregate risk assessment estimates risks likely to result from 1 to 6 months exposure to myclobutanil residues in food, drinking water, and residential pesticide scenarios. In aggregating intermediate-term risk, HED considered background chronic

dietary exposure (food and drinking water; see Table 5.1.3.1) and intermediate-term, non-dietary oral and/or dermal exposures.

For adults, intermediate-term post-application exposures may result from dermal contact with treated fruits and vegetables at "pick your own" gardens, treated home fruit and vegetable gardens and treated turf. As mentioned previously, since myclobutanil is applied at 7- to 14-day intervals, only short-term exposure is expected for the residential handler. Therefore, no aggregate intermediate-term exposure for the adult handler was performed. For toddlers, intermediate-term dermal and non-dietary oral post-application exposures may result from dermal contact with treated turf as well as non-dietary ingestion/hand-to-mouth transfer of residues from turf grass.

However, as the NOAEL (10 mg/kg/day) from a 2-generation reproduction toxicity study in rats was used for assessing short- and intermediate-term dermal, inhalation and incidental oral exposures, the short-and intermediate-term aggregate risk estimates from the post-application exposure scenarios are the same for the general U.S. population and children/toddlers (see Table 6.3.1).

Table 6.3.1. Short- and Intermediate-Term Aggregate Risk Calculations for Myclobutanil.

Population Subgroups	Exposure Scenario	NOAEL (mg/kg/day)	Level of Concern[1]	Max Exposure[2] (mg/kg/day)	Average Dietary Exposure (mg/kg/day)	Residential Exposure[3] (mg/kg/day)	Aggregate MOE (dietary and residential)[4]
Short-Term Handler Exposures							
General U.S Population	Hose End Sprayer - Mix your own	10	100	0.1	0.002587	0.054	180
Short- and Intermediate-Term Post-Application Exposures							
General U.S Population	Home Gardens	10	100	0.1	0.002587	0.031	300
	"Pick Your Own" Fruit Trees					0.09	110
	Turf - Heavy Yardwork (0.62 lb ai/A rate)					0.076	130
	Turf -Playing Golf (0.62 lb ai/A rate)[5]					0.0052	1300
Children 1-2 years old	Turf - Playing on Lawn (0.62 lb ai/A rate)[5]				0.006129	0.0695	130

[1] The level of concern (target MOE) includes 10X for interspecies extrapolation and 10X for intraspecies variation.
[2] Maximum Exposure (mg/kg/day) = NOAEL/Target MOE
[3] Residential Exposure = [Oral exposure + Dermal exposure + Inhalation Exposure].
[4] Aggregate MOE = [NOAEL ÷ (Avg Dietary Exposure + Residential Exposure)].
[5] The labels have been revised to include a maximum turf application rate of 0.62-0.68 lb ai/A. Although the residential exposure assessment was conducted using an application rate of 0.62 lb ai/A, the 0.68 lb ai/A application rate does not have a significant affect on the short-and intermediate term aggregate assessment. The MOEs do not exceed HED's level of concern.

6.4 Chronic Aggregate Risk Assessment (Food and Drinking Water): The chronic aggregate risk assessment takes into account average exposure estimates from dietary consumption of myclobutanil (food and drinking water) and residential uses. However, due to the use patterns, no chronic residential exposures are expected. Therefore, the chronic aggregate risk assessment includes exposure from food and drinking water only. The chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (9.5% of the cPAD) and all population subgroups (see Table 5.1.3.1). The most highly exposed population subgroup is children 1-2 years old at 23% of the cPAD. Therefore, the chronic aggregate risk associated with the proposed uses of myclobutanil does not exceed HED's level of concern for the general U.S. population or any population subgroups.

7.0 Cumulative

The Agency did not perform a cumulative risk assessment as part of this tolerance action for myclobutanil. However, the Agency does have concern about potential toxicity to 1,2,4-triazole and two conjugates, triazole alanine and triazole acetic acid, metabolites common to most of the triazole fungicides. To support the extension of existing parent triazole-derivative fungicide tolerances, EPA conducted an interim human health assessment for aggregate exposure to 1,2,4-triazole (M. A. Doherty, "Interim Human Health Risk Assessment of 1,2,4-Triazole to Support Tolerance Extensions and New Section 18 Soybean Tolerances for Triazole-Derivative Fungicides," June 29, 2004, DP# 304288). The exposure and risk estimates presented in this assessment are overestimates of actual likely exposures and therefore, should be considered to be highly conservative. Based on this assessment the EPA concluded that for all exposure durations and population subgroups, aggregate exposures to 1,2,4-triazole are not expected to exceed its level of concern. This assessment should be considered interim due to the ongoing series of studies being conducted by the U.S. Triazole Task Force (USTTF). Those studies are designed to provide the Agency with more complete toxicological and residue information for free triazole and are expected to be submitted to the Agency in the future. Upon completion of review of these data, EPA will prepare a more sophisticated assessment based on the revised toxicological and exposure databases.

8.0 Occupational Exposure

The occupational residential exposure assessment was conducted in the HED-memorandum dated 01/20/06 (M. Dow; D323673).

8.1 Occupational Handler Exposure and Risk

The most highly exposed occupational pesticide handlers are expected to be mixer/loaders using open-pour loading in support of aerial and ground operations and applicators using open-cab, ground-boom sprayers and aircraft. HED typically expects occupational handlers to experience short-term duration exposures (1-30 days) since only two applications per season are allowed. Although there are potentially millions of acres of soybeans that may be treated on a national basis, that acreage would be divided among a large number of commercial applicators as well as private, grower applicators. In addition, there are quite a number of other materials intended for

use against this particular soybean disease organism. Therefore, the likelihood of commercial applicators having intermediate-term duration exposures (1-6 months) is diminished. However, ExpoSAC maintains that it is possible for commercial occupational pesticide handlers to experience intermediate-term duration exposures.

In some cases, HED believes that certain individuals (private growers versus commercial applicators) may perform all three activities, that is, mix, load, and apply the material. The available exposure data for combined mixer/loader/applicator scenarios are limited in comparison to the monitoring of these two activities separately. These exposure scenarios are outlined in the PHED Surrogate Exposure Guide (August 1998). HED has adopted a methodology to present the exposure and risk estimates separately for the job functions in some scenarios and to present them as combined in other cases. Most exposure scenarios for hand-held equipment (such as hand wands, backpack sprayers, and push-type granular spreaders) are assessed as a combined job function. With these types of hand held operations, it is assumed that all handling activities are conducted by the same individual. The available monitoring data support this and HED presents them in this way. Conversely, for equipment types such as fixed-wing aircraft, ground-boom tractors, or air-blast sprayers, the applicator exposures are assessed and presented separately from those of the mixers and loaders. By separating the two job functions, HED determines the most appropriate levels of personal protective equipment (PPE) for each aspect of the job without requiring an applicator to wear unnecessary PPE that may be required for a mixer/loader (*e.g.*, chemical-resistant gloves may only be necessary during the pouring of a liquid formulation).

Chemical-specific data were not available with which to assess pesticide handler exposure. Therefore, surrogate data from studies in the PHED Surrogate Exposure Guide (Version 1.1; August 1998) were used to estimate mixer/loader and applicator exposure.

For pesticide handlers, it is HED practice to present estimates of dermal exposure for "baseline"; that is, with a single layer of work clothing consisting of a long sleeved shirt, long pants, shoes plus socks and no protective gloves and for "baseline" **and the use** of protective gloves or other PPE as might be necessary. See Table 8.1.1 for a summary of exposures and risks to occupational pesticide handlers.

Table 8.1.1. Summary of Exposures and Risks to Occupational Handlers Applying Myclobutanil to Soybean.

Unit Exposure[1] (mg ai/lb handled)	Application Rate[2] (lb ai/A)	Units Treated[3] Per Day (A)	ADD[4] (mg ai/kg bw/day)	NOAEL[5] (mg ai/kg w/day)	Combined MOE[6]
Mixer/Loader – Liquid Open Pour					
Dermal: No Glove 2.9 LC W Glove 0.023 MC Inhal. 0.0012 HC	0.125	1200	Dermal: No Glove 3.1 W Glove 0.0245 Inhal 0.0026	Dermal 10 Inhalation 10	Dermal: No Glove 3.2 W Glove 370
Applicator – Ground-boom – open cab					
Dermal: No Glove 0.014 HC W Glove 0.014 MC Inhal 0.00074 HC	0.125	200	Dermal: No Glove 0.0025 W Glove 0.0025 Inhal 0.00026	Dermal 10 Inhalation 10	Dermal: No Glove 1,900 W Glove 1,900
Aerial Applicator					
Dermal: No Glove 0.0050 MC Inhal 0.000068 HC	0.125	1200	Dermal: No Glove 0.00535 Inhal 0.00015	Dermal 10 Inhalation 10	Dermal: No Glove 1,800

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Dermal = Single Layer Work Clothing **No Gloves**; Single Layer Work Clothing **With Gloves**; Inhal. = Inhalation. Units = mg ai/pound of active ingredient handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.
2. Applic. Rate. = Taken from the Laredo® supplemental labeling.
3. Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; SOP No. 9.1. Science Advisory Council for Exposure; Revised 5 July 2000.
4. Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated * 0.5 (% dermal exposure) ÷ Body Weight (70 kg).
5. NOAEL = No Observable Adverse Effect Level: short- and intermediate-term dermal and inhalation NOAEL = 10 mg ai/kg bw/day
6. Combined Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. Since the dermal and inhalation toxicological effects are the same and are identified from the same study, the dermal and inhalation exposures are summed, then divided into the NOAEL.

A MOE of 100 is adequate to protect occupational pesticide handlers. Provided handlers wear protective gloves where applicable, (pilots are not required), the MOEs are >100 and the proposed use does not exceed HED's level of concern.

8.2 Occupational Post-Application Exposure: There is a potential for agricultural workers to experience post-application exposures to pesticides during the course of typical agricultural activities. HED in conjunction with the Agricultural Re-entry Task Force (ARTF) has identified a number of post-application agricultural activities that may occur. HED has also identified transfer coefficients (TC) expressed as cm^2/hr, which describe the amount of foliar dislodgeable pesticide residue that is available to be transferred to agricultural workers during the course of post-application agricultural activities.

There were no chemical specific data with which to estimate post-application exposures of agricultural workers to dislodgeable residues of myclobutanil. Therefore, theoretical estimates of exposure, based on surrogate studies, have been conducted. The ExpoSAC (SOP 003.1, Rev. 7 Aug. 2000, Regarding Agricultural Transfer Coefficients; Amended ExpoSAC Meeting notes - 13 Sept 01) lists a number of possible post-application agricultural activities relative to soybeans that result in pesticide exposure to agricultural workers. TCs are identified for each of the post-application, agricultural activities. The TCs are derived from data in surrogate exposure studies conducted during the various activities listed.

The highest TC identified for soybeans is for scouting or irrigation activities with a TC of 1,500 cm^2/hr. For this assessment, HED uses the 1,500 cm^2/hr TC for a Tier 1, screening level estimate.

The TCs used in this assessment are from an interim transfer coefficient procedure developed by HED's ExpoSAC using proprietary data from the ARTF database (SOP# 3.1). It is the intention of HED's ExpoSAC that this procedure will be periodically updated to incorporate additional information about agricultural practices in crops and new data on transfer coefficients. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.

Post-application worker exposure is estimated using HED procedure that assumes 20% of the application rate is available as dislodgeable foliar residue on the day of treatment. HED expects post-application agricultural exposures to scouts (*i.e.*, crop advisors) or workers involved in irrigation would typically be short-term.

PDR_t = DFR_t * CF1 * Tc * ET where:
PDR_t = potential dose rate on day "t" (mg/day)
DFR_t = dislodgeable foliar residue on day "t" ($\mu g/cm^2$)
CF1 = weight unit conversion factor to convert µg units in DFR value to mg for the daily dose (0.001 mg/µg)
TC = transfer coefficient (cm^2/hr) (In this case 1,500 cm^2/hr; ExpoSAC SOP 003.1 Rev. 7 Aug. 2000; amended 13 Sept 01 ExpoSAC meeting Notes).
ET = Exposure Time (hrs) (8)

and

DFR_t = AR * F * $(1\text{-}D)^t$ * CF2 * CF3 where:

AR = Application rate (lb ai/A) (0.125 lb ai/A)
F = fraction of ai retained on foliage (unitless)
D = fraction of residue that dissipates daily (unitless)
t = post-application day on which exposure is being assessed
CF2 = weight unit conversion factor to convert the lbs ai in the application rate to µg for the DFR value (4.54×10^8 µg/lb)
CF3 = Area unit conversion factor to convert the surface area units (ft^2) in the application rate to cm^2 for the DFR value (1.08×10^{-3} ft^2/cm^2 or 2.47×10^{-8} acre/cm^2 if the application rate is per acre).

$\therefore$ DFR = 0.125 lb ai/A * 0.20 * $(1\text{-}0)^0$ * 4.54×10^8 µg ai/lb * 2.47×10^{-8} A/cm^2 = 0.28 $\mu g/cm^2$

PDR = 0.28 $\mu g/cm^2$ * 0.001 mg/µg * 1,500 cm^2/hr * 8 hr/day = 3.36 mg ai/day * 0.5 (% dermal absorption) ÷ 70 kg bw = 0.024 mg ai/kg bw/day

MOE = NOAEL ÷ PDR
$\therefore$ 10 mg ai/kg bw/day ÷ 0.024 mg ai/kg bw/day = 416.

An MOE of 100 is adequate to protect agricultural workers from post-application exposure to myclobutanil. The calculated MOE >100, and, therefore, does not exceed HED's level of concern.

8.3 REI: Myclobutanil is classified in Acute Toxicity Category IV for acute dermal, acute inhalation and primary skin irritation. It is classified in Category I for primary eye irritation and it is a "positive" dermal sensitizer. Therefore the interim Worker Protection Standard (WPS) REI of 24 hours is adequate to protect agricultural workers. The Laredo® label lists the REI as 24 hours.

Title 40 of the Code of Federal Regulations, § 156.208 (c) (2) states: If a product contains only one active ingredient and it is in Toxicity Category I by the criteria in paragraph (c) (1) of this section, the restricted-entry interval shall be 48 hours." The Federal Register Vol. 57, No. 163, 21 August 1992 page 38104 and 38142 (For 40 CFR Parts 156 and 170) indicates that "...a 48-hour REI is established for any product containing an active ingredient that is in Toxicity Category I (most acutely toxic category) because of dermal toxicity or skin or eye irritation." **HED suggests that the RD confirm or correct, as may be necessary, the 24-hour REI listed on the product label.**

9.0 Data Needs and Label Requirements

9.1 Toxicology

- None.

9.2 Residue Chemistry

- Revised Section F to include the following HED-recommended tolerances and corresponding correct commodity definitions: soybean, seed (0.25 ppm); soybean, forage (3.5 ppm); soybean, hay (15 ppm); aspirated grain fractions (35 ppm), and soybean, refined oil (0.40 ppm).
- Information on the maximum storage intervals of samples in the processed food and feed study, from harvest to analysis, for soybean seed (RAC), hulls, meal and refined oil.

9.3 Occupational/Residential Exposure

- HED suggests that the RD confirm or correct, as may be necessary, the 24 hour REI listed on the product label.

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